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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,316	01/23/2004	Michael J. Borrelli	10546-109	8323

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,316	BORRELLI, MICHAEL J.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *14-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,8,9 and 11-13* is/are rejected.

7)☒ Claim(s) *4,7 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I, claims 2-5 and 8-13 in the reply filed on 07/27/2006 is acknowledged. Although Applicants state the election is with traverse, Applicants have not provided any argument against the restriction requirement. However, upon examination of the instant invention, it was found that the inventions of groups II-IV were related to the elected invention and thus the groups II-IV, claims 1-17, will be examined with the elected invention.

The restriction requirement between groups I-IV and group V is made FINAL for the reasons set forth in the Office action filed 05/02/2006.

Status of the Application

Claims 1-32 are pending. Claims 1-17 and new claim 32 are currently under examination. Claims 18-31 are withdrawn as being drawn to a non-elected invention.

Claim Objections

Claims 4, 7 and 10 are objected to as being dependent upon a rejected base claim and reciting non-elected subject matter, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-6, 8-9, 11-13 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (US 2005/0032726), Frisan et al. (Int. J. Med. Microbiol. 2002), Sert et al. (Oncogene 1999) and Xu et al. (Clinical Cancer Research 2001).

The instant claims are drawn to a gene therapy vector comprising a first polynucleotide encoding a gene for B subunit of a cytolethal distending toxin (CDT) and a second polynucleotide encoding an antisense oligonucleotide that inhibits expression of a sense oligonucleotide encoding a DNA repair protein, wherein the first and second polynucleotides are operably linked to an inducible promoter. The claims are further drawn to a heat shock promoter, an inducible promoter having a nucleotide sequence of SEQ ID NO.7, a gene selected from the group as listed in claim 5, a gene having a nucleotide sequence of SEQ ID NO.5, wherein said DNA repair protein is ku70 and wherein the vector is a viral vector such as adenovirus.

Li et al. teach an expression vector comprising a heat shock promoter operably linked to an antisense compound targeted to a gene encoding a DNA repair protein ku70 wherein said antisense compound reduces expression of ku70 (see paragraph 0010). Li et al. teach said DNA repair protein ku70 plays a role in DNA repair and

inhibition of ku70 in a cancer cell increase the sensitivity of the cancer cell to heat, chemical or radiation-induced DNA damage (see paragraph 0010). Li et al. teach the antisense oligonucleotide can be expressed from an adenoviral vector (see paragraph 0058). Li et al. does not teach a gene therapy vector comprising a CDT.

Xu et al. teach strategies for cancer therapy comprising administering toxins to cancer cells wherein the toxin, in response to a prodrug, causes cancer cell death.

Frisan et al. teach CDTs having the ability to induce cell cycle arrest or apoptosis in mammalian cells (see page 495). Frisan et al. teach a CDT activity is linked to three genes, *cdtA, cdtB* and *cdtC* and expression of all three genes in cells elicit cell toxicity and cell cycle arrest. Frisan et al. teach the *C. jejuni* cdtB has specific Dnase-I activity which induces DNA damage. Frisan et al. teach that CDTs work at the nuclear level causing DNA damage and CDTs can be used as immunotoxins as a complement in cancer treatment. Frisan et al. further teach CDTs interference with the cell cycle makes them a very good candidate as an anti-tumor agent (see page 499). Similarly Sert et al. teach CDTs, particularly *E. coli* CDT (which comprises *cdtA, cdtB* and *cdtC)* cell cycle arrest and DNA damage (see Figures 4 and 5 and page 6302).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a toxic gene into a gene therapy vector comprising an antisense targeted to a DNA repair protein.

One would have been motivated to use a CDT toxic gene as taught by Frisan et al. and Sert et al. for purpose of treating cancer because Frisan et al. teach CDTs are good anti-tumor agents. One would have been motivated to use a toxin gene along with

an antisense targeted to a DNA repair gene because Li et al. teach inhibition of a DNA repair agent using an antisense makes the cell more sensitive for additional therapies since the cancer cell is unable to rely on the internal repair mechanism, such as through a DNA repair protein. One would have been further motivated to use a toxin, such as CDT, in a gene therapy vector for the treatment of cancer because Frisan et al. teach CDTs can be used as immunotoxins to complement cancer treatment. Further, one would have been further motivated to use a toxin such as CDT because, although Xu et al. teach cancer treatment using a toxin that is activated by a prodrug is an effective treatment to elicit cancer cell death, there are major limitations of such treatments: 1) most toxins are dependent on replication of cells to work and because many tumor cells are in a non-proliferating state the prodrug needs to work on nondividing cells and 2) the toxins can be active in nontumor tissues, causing cell death in normal tissue. Frisan et al. and Sert et al. teach CDTs do not require an additional prodrug for activation and therefore can be specifically delivered to the desired cell for induction of DNA damage.

Finally, one would have had a reasonable expectation of success given Frisan et al. and Sert et al. teach CDTs cause cell cycle arrest and DNA damage when delivered to cells and given that Xu et al. teach toxins delivered to cells are an effective treatment against proliferating cancer cells. Further, one would have had a reasonable expectation of success because Li et al. specifically teach inhibition of expression of a DNA repair protein using an antisense gene increases the cells sensitivity to further chemical treatments.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong
Examiner
Art Unit 1635

SEAN McGARRY
PRIMARY EXAMINER
1635